Treatment with etanercept and low monocyte concentration contribute to the risk of invasive aspergillosis in patients post allogeneic stem cell transplantation.

Zoran T, Weber M, Springer J, White PL, Bauer J, Schober A, Löffler C, Seelbinder B, Hünniger K, Kurzai O, Scherag A, Schäuble S, Morton CO, Einsele H, Linde J, Löffler J (2019) Treatment with etanercept and low monocyte concentration contribute to the risk of invasive aspergillosis in patients post allogeneic stem cell transplantation. *Sci Rep* 9(1), 17231.

Details

Abstract

Invasive aspergillosis (IA) is a life-threatening complication among allogeneic hematopoietic stem cell transplant (alloSCT) recipients. Despite well known risk factors and different available assays, diagnosis of invasive aspergillosis remains challenging. 103 clinical variables from patients with hematological malignancies and subsequent alloSCT were collected. Associations between collected variables and patients with (n = 36) and without IA (n = 36) were investigated by applying univariate and multivariable logistic regression. The predictive power of the final model was tested

in an independent patient cohort (23 IA cases and 25 control patients). Findings were investigated further by in vitro studies, which analysed the effect of etanercept on A. fumigatus-stimulated macrophages at the gene expression and cytokine secretion. Additionally, the release of C-X-C motif chemokine ligand 10 (CXCL10) in patient sera was studied. Low monocyte concentration ($p = 4.8 \times 10\text{-}06$), severe GvHD of the gut (grade 2-4) ($p = 1.08 \times 10\text{-}02$) and etanercept treatment of GvHD ($p = 3.5 \times 10\text{-}03$) were significantly associated with IA. Our studies showed that etanercept lowers CXCL10 concentrations in vitro and ex vivo and down-regulates genes involved in immune responses and TNF-alpha signaling. Our study offers clinicians new information regarding risk factors for IA including low monocyte counts and administration of etanercept. After necessary validation, such information may be used for decision making regarding antifungal prophylaxis or closely monitoring patients at risk.

Involved units

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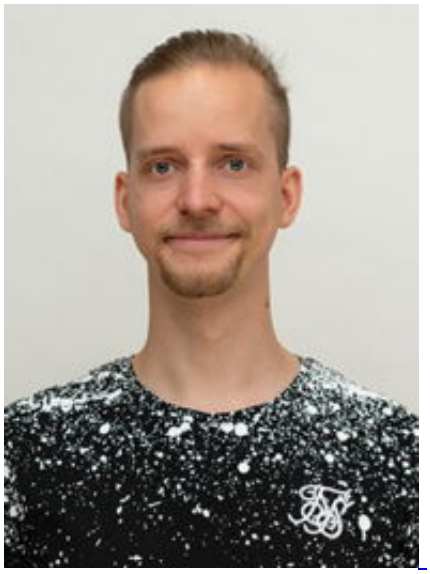

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Topics

Disease Systems Biology

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